

IN THE SPECIFICATION

- (1) Replace the paragraph at page 1, lines 3-7 with the following paragraph.

This application is a division of co-pending application Serial No. 09/879,792 filed June 13, 2001, which claims the benefit of and incorporates by reference co-pending provisional applications Serial No. 60/211,224 filed June 13, 2000, Serial No. 60/283,353 filed April 13, 2001, and Serial No. 60/283,648 filed April 16, 2001, and PCT Application [[_____]] PCT/EP01/06618 filed June 12, 2001. The entirety of each of these applications is expressly incorporated herein by reference.

- (2) Replace the paragraph at page 2, lines 9-13 with the following substitute paragraph.

[05] One embodiment of the invention is a cDNA encoding a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof.

- (3) Replace the paragraph at page 2, lines 14-19 with the following substitute paragraph.

Yet another embodiment of the invention is an expression vector comprising a polynucleotide which encodes a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof.

- (4) Replace the paragraph at page 2, lines 20-24 with the following substitute paragraph.

Another embodiment of the invention is a host cell comprising an expression vector which encodes a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof.

- (5) Replace the paragraph at page 2, lines 25-29 with the following substitute paragraph.

Still another embodiment of the invention is a purified polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof.

- (6) Replace the paragraph at page 3, lines 1-5 with the following substitute paragraph.

Even another embodiment of the invention is a fusion protein comprising a polypeptide consisting of an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof.

- (7) Replace the paragraph at page 3, lines 6-12 with the following substitute paragraph.

Another embodiment of the invention is a method of producing a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid

sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof. A host cell comprising an expression vector that encodes the polypeptide is cultured under conditions whereby the polypeptide is expressed. The polypeptide is isolated.

- (8) Replace the paragraph at page 3, lines 13-26 with the following substitute paragraph.

Yet another embodiment of the invention is a method of detecting a coding sequence for a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof. A polynucleotide comprising 11 contiguous nucleotides selected from the group consisting of (a) the complement of the nucleotide sequence shown in SEQ ID NO:11, (b) the complement of the coding sequence of the cDNA insert of plasmid pCRII-TMSP3, (c) a polynucleotide that hybridizes under stringent conditions to (a) or (b), (d) a polynucleotide having a nucleic acid sequence that deviates from the nucleic acid sequences specified in (a) to (c) due to the degeneration of the genetic code, and (e) a polynucleotide that represents a fragment, derivative, or allelic variation of a nucleic acid sequence specified in (a) to (d) is hybridized to nucleic acid material of a biological sample to form a hybridization complex. The hybridization complex is detected.

- (9) Replace the paragraph at page 3, line 27 to page 4, line 12 with the following substitute paragraph.

Even another embodiment of the invention is a kit for detecting a coding sequence for a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[____]] PTA-3433), and (c) biologically active variants thereof. The kit comprises a polynucleotide and instructions for detecting the coding sequence. The polynucleotide comprises 11 contiguous nucleotides selected from the group consisting of (a) the complement of the nucleotide sequence shown in SEQ ID NO:11, (b) the complement of the coding sequence of the cDNA insert of plasmid pCRII-TMSP3 to nucleic acid material of a biological sample to form a hybridization complex, (c) a polynucleotide that hybridizes under stringent conditions to (a) or (b), (d) a polynucleotide having a nucleic acid sequence that deviates from the nucleic acid sequences specified in (a) to (c) due to the degeneration of the genetic code, and (e) a polynucleotide that represents a fragment, derivative, or allelic variation of a nucleic acid sequence specified in (a) to (d).

- (10) Replace the paragraph at page 4, lines 13-19 with the following substitute paragraph.

Still another embodiment of the invention is a method of detecting a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. PTA-3433), and (c) biologically active variants thereof. A biological sample is contacted with a reagent that specifically binds to the polypeptide to form a reagent-polypeptide complex. The reagent-polypeptide complex is detected.

- (11) Replace the paragraph at page 4, lines 20-25 with the following substitute paragraph.

Yet another embodiment of the invention is a kit for detecting a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof. The kit comprises an antibody which specifically binds to the polypeptide and instructions for detecting the polypeptide.

- (12) Replace the paragraph at page 4, lines 26 to page 5, line 5 with the following substitute paragraph.

Even another embodiment of the invention is a method of screening for agents that can regulate an activity of a human transmembrane serine protease. A test compound is contacted with a polypeptide comprising an amino acid sequence selected from the group consisting of: (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof. Binding of the test compound to the polypeptide is detected. A test compound that binds to the polypeptide is thereby identified as a potential agent for regulating the activity of the human transmembrane serine protease.

- (13) Replace the paragraph at page 5, lines 6-17 with the following substitute paragraph.

A further embodiment of the invention is a method of screening for therapeutic agents that can regulate an enzymatic activity of a human transmembrane serine protease. A test compound is contacted with a polypeptide comprising an amino acid sequence selected

from the group consisting of: (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[____]] PTA-3433), and (c) biologically active variants thereof. The enzymatic activity of the polypeptide is detected. A test compound that increases the enzymatic activity of the polypeptide is thereby identified as a potential therapeutic agent for increasing the enzymatic activity of the human transmembrane serine protease. A test compound that decreases the enzymatic activity of the polypeptide is thereby identified as a potential therapeutic agent for decreasing the enzymatic activity of the human transmembrane serine protease.

- (14) Replace the paragraph at page 5, lines 18-27 with the following substitute paragraph.

Still another embodiment of the invention is a method of screening for therapeutic agents that can regulate an activity of a human transmembrane serine protease. A test compound is contacted with a product encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[____]] PTA-3433), and (c) biologically active variants thereof. Binding of the test compound to the product is detected. A test compound that binds to the product is thereby identified as a potential therapeutic agent for regulating the activity of the human transmembrane serine protease.

- (15) Replace the paragraph at page 5, line 28 to page 6, line 6 with the following substitute paragraph.

Another embodiment of the invention is a method of reducing an activity of a human transmembrane serine protease. A cell comprising the human transmembrane serine protease is contacted with a reagent that specifically binds to a product encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[____]] PTA-3433), and (c) biologically active variants thereof. The activity of the human transmembrane serine protease is thereby reduced.

- (16) Replace the paragraph at page 6, lines 7-12 with the following substitute paragraph.

Yet another embodiment of the invention is a pharmaceutical composition, comprising a reagent and a pharmaceutically acceptable carrier. The reagent specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[____]] PTA-3433), and (c) biologically active variants thereof; and

- (17) Replace the paragraph at page 6, lines 13-19 with the following substitute paragraph.

Even another embodiment of the invention is a pharmaceutical composition comprising a reagent and a pharmaceutically acceptable carrier. The reagent specifically binds to a product of a polynucleotide comprising a coding sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[____]] PTA-3433), and (c) biologically active variants thereof.

- (18) Replace the paragraph at page 6, lines 20-25 with the following substitute paragraph.

A further embodiment of the invention is a pharmaceutical composition comprising an expression vector and a pharmaceutically acceptable carrier. The expression vector encodes a polypeptide comprising an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof.

- (19) Replace the paragraph at page 6, line 26 to page 7, line 7 with the following substitute paragraph.

Still another embodiment of the invention is a method of treating a disorder selected from the group consisting of chronic obstructive pulmonary disease, cancer, metastasis of malignant cells, tumor angiogenesis, inflammation, atherosclerosis, neurodegenerative diseases, and pathogenic infections. A therapeutically effective dose of a reagent that inhibits a function of a human transmembrane serine protease is administered to a patient in need thereof. The human transmembrane serine protease comprises an amino acid sequence selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), and (c) biologically active variants thereof. Symptoms of the disorder are thereby ameliorated.

- (20) Replace the paragraph at page 7, lines 8-19 with the following substitute paragraph.

Even another embodiment of the invention is a isolated polynucleotide selected from the group consisting of: (a) a polynucleotide encoding a protein that comprises the amino acid sequence of SEQ ID NO:12, (b) a polynucleotide comprising the sequence of SEQ ID NO:11, (c) a polynucleotide comprising a coding sequence of a cDNA contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), (d) a polynucleotide encoding a protein that comprises the amino acid sequence encoded by the cDNA of plasmid pCRII-TMSP3, (e) a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in (a) - (d); (e) a polynucleotide having a nucleic acid sequence that deviates from the nucleic acid sequences specified in (a) - (d) due to the degeneration of the genetic code, and (f) a polynucleotide that represents a fragment, derivative, or allelic variation of a nucleic acid sequence specified in (a) - (e).

- (21) Replace the paragraph at page 7, line 20 to page 8, line 2 with the following substitute paragraph.

Yet another embodiment of the invention is an expression vector comprising polynucleotide selected from the group consisting of: (a) a polynucleotide encoding a protein that comprises the amino acid sequence of SEQ ID NO:12, (b) a polynucleotide comprising the sequence of SEQ ID NO:11, (c) a polynucleotide comprising a coding sequence of a cDNA contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), (d) a polynucleotide encoding a protein that comprises the amino acid sequence encoded by the cDNA of plasmid pCRII-TMSP3, (e) a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified

in (a) - (d); (e) a polynucleotide having a nucleic acid sequence that deviates from the nucleic acid sequences specified in (a) - (d) due to the degeneration of the genetic code, and (f) a polynucleotide that represents a fragment, derivative, or allelic variation of a nucleic acid sequence specified in (a) - (e).

- (22) Replace the paragraph at page 8, lines 3-14 with the following substitute paragraph.

A further embodiment of the invention is a host cell comprising an expression vector comprising polynucleotide selected from the group consisting of: (a) a polynucleotide encoding a protein that comprises the amino acid sequence of SEQ ID NO:12, (b) a polynucleotide comprising the sequence of SEQ ID NO:11, (c) a polynucleotide comprising a coding sequence of a cDNA contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[_____]] PTA-3433), (d) a polynucleotide encoding a protein that comprises the amino acid sequence encoded by the cDNA of plasmid pCRII-TMSP3, (e) a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in (a) - (d); (e) a polynucleotide having a nucleic acid sequence that deviates from the nucleic acid sequences specified in (a) - (d) due to the degeneration of the genetic code, and (f) a polynucleotide that represents a fragment, derivative, or allelic variation of a nucleic acid sequence specified in (a) - (e).

- (23) Replace the paragraph at page 8, lines 15-19 with the following substitute paragraph.

Another embodiment of the invention is a preparation of antibodies that specifically bind to a polypeptide selected from the group consisting of (a) the amino acid sequence shown in SEQ ID NO:12, (b) the amino acid sequence encoded by a cDNA insert contained

within plasmid pCRII-TMSP3 (ATCC Accession No. [[____]] PTA-3433), and
(c) biologically active variants thereof.

- (24) Replace the paragraph at page 8, line 20 to page 9, line 2 with the following substitute paragraph.

Even another embodiment of the invention is a antisense oligonucleotide that hybridizes to a polynucleotide selected from the group consisting of (a) a polynucleotide encoding a protein that comprises the amino acid sequence of SEQ ID NO:12, (b) a polynucleotide comprising the sequence of SEQ ID NO:11, (c) a polynucleotide comprising a coding sequence of a cDNA contained within plasmid pCRII-TMSP3 (ATCC Accession No. [[____]] PTA-3433), (d) a polynucleotide encoding a protein that comprises the amino acid sequence encoded by the cDNA of plasmid pCRII-TMSP3, (e) a polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in (a) - (d); (e) a polynucleotide having a nucleic acid sequence that deviates from the nucleic acid sequences specified in (a) - (d) due to the degeneration of the genetic code, and (f) a polynucleotide that represents a fragment, derivative, or allelic variation of a nucleic acid sequence specified in (a) - (e).